## CLAIMS

**What is claimed is:**

1. A method of inhibiting agonist-induced down-regulation of a G protein-coupled receptor, the method comprising contacting cells comprising the G protein-coupled receptor with an effective amount of an inhibitor, wherein:

the G protein-coupled receptor is one that specifically binds to a polypeptide having the amino acid sequence of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2);

the inhibitor reduces specific binding of the G protein-coupled receptor to said polypeptide; and

an effective amount is an amount sufficient to reduce agonist-induced down-regulation of the G protein-coupled receptor in the cells.

2. The method of claim 1, wherein the inhibitor comprises a polypeptide that reduces agonist-induced down-regulation of the G protein-coupled receptor and comprises an amino acid sequence that has at least about 70% identity to GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2) over a comparison window of at least 15 contiguous amino acids.

3. The method of claim 2, wherein the amino acid sequence has at least about 95% identity to GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2) over a comparison window of at least 15 contiguous amino acids.

4. The method of claim 3, wherein the amino acid sequence comprises an amino acid subsequence of at least about 500 amino acids, of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2).

5. The method of claim 2, wherein identity is determined by a sequence alignment performed using BLASTP with default parameters set to measure 70% identity.

6. The method of claim 2, wherein the amino acid sequence defines a peptide that specifically binds to a G protein-coupled receptor.

7. The method of claim 6, wherein the peptide comprises a subsequence of at least about 500 amino acids of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2).

8. The method of claim 6, wherein the peptide reduces agonist-induced down-regulation of the G protein-coupled receptor.

9. The method of claim 8, wherein the peptide reduces agonist-induced down-regulation by at least about 20%, as determined by a radioligand binding assay.

10. The method of claim 2, wherein said contacting comprises administering a composition comprising the polypeptide to the cells.

11. The method of claim 2, wherein said contacting comprises administering a composition comprising a polynucleotide encoding the polypeptide to the cells, whereby said administration results in the expression of the polypeptide.

12. The method of claim 1, wherein the cells are *in vitro*.

13. The method of claim 1, wherein the cells are *in vivo*.

14. The method of claim 1, wherein the G protein-coupled receptor is selected from the group comprising the delta opioid receptor, the kappa opioid receptor, the D2 dopamine receptor, the D4 dopamine receptor, the beta 2 adrenergic receptor, the NK1 (substance P) receptor, the bradykinin B1 receptor, and US28.

15. The method of claim 14, wherein G protein-coupled receptor is selected from the group comprising the delta opioid receptor, the kappa opioid receptor, the D2 dopamine receptor, the D4 dopamine receptor, the NK1 (substance P) receptor, the bradykinin B1 receptor, and US28.

16. The method of claim 15, wherein said contacting is performed by administering a composition comprising the inhibitor to a subject in need of pain reduction.

17. The method of claim 1, additionally comprising contacting the cells with an agonist of the G protein-coupled receptor in an amount sufficient to stimulate the G protein-coupled receptor.

18. A method of enhancing agonist-induced down-regulation of a G protein-coupled receptor, the method comprising contacting cells comprising the G protein-coupled receptor with an effective amount of a polypeptide that increases agonist-induced down-regulation of the G protein-coupled receptor, wherein:

the G protein-coupled receptor is one that specifically binds to a polypeptide having the amino acid sequence of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2);

the polypeptide comprises an amino acid sequence that has at least about 70% identity to GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2) over a comparison window of at least 15 contiguous amino acids; and

an effective amount is an amount sufficient to increase agonist-induced down-regulation of the G protein-coupled receptor in the cells.

19. The method of claim 18, wherein the amino acid sequence has at least about 95% identity to GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2) over a comparison window of at least 15 contiguous amino acids.

20. The method of claim 18, wherein identity is determined by a sequence alignment performed using BLASTP with default parameters set to measure 70% identity.

21. The method of claim 18, wherein the amino acid sequence defines a polypeptide or peptide that specifically binds to a G protein-coupled receptor.

22. The method of claim 21, wherein the polypeptide or peptide increases agonist-induced down-regulation of the G protein-coupled receptor.

23. The method of claim 22, wherein the peptide increases agonist-induced down-regulation by at least about 20%, as determined by a radioligand binding assay.

24. The method of claim 18, wherein said contacting comprises administering a composition comprising the polypeptide to the cells.

25. The method of claim 18, wherein said contacting comprises administering a composition comprising a polynucleotide encoding the polypeptide to the cells, whereby said administration results in the expression of the polypeptide.

26. The method of claim 18, wherein the cells are *in vitro*.

27. The method of claim 18, wherein the cells are *in vivo*.

28. The method of claim18, wherein the wherein the G protein-coupled receptor is selected from the group comprising the delta opioid receptor, the kappa opioid receptor, the D2 dopamine receptor, the D4 dopamine receptor, the beta 2 adrenergic receptor, the NK1 (substance P) receptor, the bradykinin B1 receptor, and US28.

29. The method of claim18, additionally comprising contacting the cells with an agonist of the G protein-coupled receptor in an amount sufficient to stimulate the G protein-coupled receptor.

30. An isolated polypeptide comprising an amino acid sequence, wherein the amino acid sequence has at least about 70% identity to GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2) over a comparison window of at least 15 contiguous amino acids.

31. The polypeptide of claim 30, wherein the amino acid sequence has at least about 95% identity to GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2) over a comparison window of at least 15 contiguous amino acids.

32. The polypeptide of claim 30, wherein the amino acid sequence comprises an amino acid sequence, or subsequence of at least about 500 amino acids, of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2).

33. The polypeptide of claim 30, wherein identity is determined by a sequence alignment performed using BLASTP with default parameters set to measure 70% identity.

34. The polypeptide of claim30, wherein the amino acid sequence defines a polypeptide or a peptide that specifically binds to a G protein-coupled receptor.

35. The polypeptide of claim 34, wherein the G protein-coupled receptor is selected from the group comprising the delta opioid receptor, the kappa opioid receptor, the D2 dopamine receptor, the D4 dopamine receptor, the beta 2 adrenergic receptor, the NK1 (substance P) receptor, the bradykinin B1 receptor, and US28.

36. The polypeptide of claim 35, wherein the G protein-coupled receptor is the delta opioid receptor.

37. The polypeptide of claim 34, wherein the amino acid sequence defines a peptide that specifically binds to a G protein-coupled receptor.

38. The polypeptide of claim 37, wherein the peptide comprises a subsequence of at least about 500 amino acids of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2).

39. The polypeptide of claim 37, wherein the peptide reduces agonist-induced down-regulation of the G protein-coupled receptor.

40. The polypeptide of claim 38, wherein the peptide reduces agonist-induced down-regulation by at least about 20%, as determined by a radioligand binding assay.

41. The polypeptide of claim 30, wherein the polypeptide comprises a signal sequence.

42. The polypeptide of claim 30, wherein the polypeptide comprises an epitope tag.

43. A polypeptide comprising an amino acid sequence, wherein the amino acid sequence has at least about 70% identity to delta opioid receptor SEQ ID NO:3 over a comparison window of at least 15 contiguous amino acids and defines a peptide that specifically binds GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2),

wherein the polypeptide does not comprise more than about 50 contiguous amino acids of delta opioid receptor.

44. The polypeptide of claim 43, wherein the amino acid sequence has at least about 95% identity to delta opioid receptor SEQ ID NO:3 over a comparison window of at least 15 contiguous amino acids.

45. The polypeptide of claim 44, wherein the amino acid sequence comprises an amino acid sequence, or subsequence of at least about 30 amino acids, of delta opioid receptor SEQ ID NO:3.

46. The polypeptide of claim 43, wherein identity is determined by a sequence alignment performed using BLASTP with default parameters set to measure 70% identity.

47. An isolated polynucleotide that encodes the polypeptide of claim 30, 34, 37, 39, or 43

48. A vector that comprises that polynucleotide of claim 47.

49. The vector of claim 48, wherein the vector is an expression vector.

50. A host cell comprising the vector of claim 48.

51. A host cell comprising the vector of claim 49.

52. A method of producing a polypeptide comprising:

(a) culturing the host cell of claim 51 under conditions suitable for expression of the polypeptide; and

(b) recovering the expressed polypeptide from the culture.

53. A composition comprising the polypeptide of claim 30, 34, 37, 39, or 43 or a polynucleotide encoding said polypeptide, and a pharmaceutically acceptable carrier.

54. The composition of claim 53, wherein the composition comprises the polypeptide of claim 39 in an amount sufficient to inhibit agonist-induced down-regulation

of the G protein-coupled receptor when the composition is contacted with cells comprising the G protein-coupled receptor.

55. The composition of claim 54, additionally comprising an agonist of the G protein-coupled receptor.

56. An antibody or antiserum that specifically binds to the polypeptide of claim 30, 34, 37, 39, or 43.

57. The antibody or antiserum of claim 56, wherein the antibody or antiserum is produced by:

(a) administering said polypeptide to a mammal; and

(b) recovering the antibody or antiserum from the mammal.

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58. A method of prescreening for an agent that modulates agonist-induced down-regulation of a G protein-coupled receptor, the method comprising:

a) contacting a test agent with a polypeptide that specifically binds said G protein-coupled receptor and modulates agonist-induced down-regulation of the G protein-coupled receptor, wherein the polypeptide comprises an amino acid sequence that has at least about 70% identity to GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2) over a comparison window of at least 15 contiguous amino acids or with a polynucleotide encoding said polypeptide; and

b) detecting specific binding of the test agent to the polypeptide or polynucleotide.

59. The prescreening method of claim 58, wherein the test agent is contacted with the polypeptide in the presence of the G protein-coupled receptor or a fragment thereof that is capable of specifically binding to the polypeptide.

60. The prescreening method of claim 58, wherein said method additionally comprises recording any test agent that specifically binds to the polypeptide or polynucleotide in a database of candidate agents that may inhibit agonist-induced down-regulation of the G protein-coupled receptor.

61. The prescreening method of claim 58, wherein said detecting comprises detecting specific binding of the test agent to the polypeptide.

62. The prescreening method of claim 58, wherein said detecting comprises detecting specific binding of the test agent to the polynucleotide.

63. The prescreening method of claim 58, wherein said contacting is *in vitro*.

64. A method of prescreening for an agent that inhibits or enhances agonist-induced down-regulation of a G protein-coupled receptor, the method comprising:

a) contacting a test agent with a G protein-coupled receptor, or fragment thereof, wherein the G protein-coupled receptor or receptor fragment specifically binds to a polypeptide having the amino acid sequence of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2); and

b) detecting specific binding of the test agent to the receptor or receptor fragment.

65. The prescreening method of claim 64, wherein said method additionally comprises recording any test agent that specifically binds to the G protein-coupled receptor or receptor fragment in a database of candidate agents that may inhibit or enhance agonist-induced down-regulation of the G protein-coupled receptor.

66. The prescreening method of claim 64, wherein the G protein-coupled receptor is selected from the group comprising the delta opioid receptor, the kappa opioid receptor, the D2 dopamine receptor, the D4 dopamine receptor, the beta 2 adrenergic receptor, the NK1 (substance P) receptor, the bradykinin B1 receptor, and US28.

67. The prescreening method of claim 64, wherein said contacting is *in vitro*.

68. A method of screening for an agent that inhibits or enhances agonist-induced down-regulation of a G protein-coupled receptor, said method comprising:

a) contacting a test agent with a cell comprising:

(i) a G protein-coupled receptor, or fragment thereof, wherein the G protein-coupled receptor or receptor fragment specifically binds to a polypeptide having the amino acid sequence of GASP SEQ ID NO:2 (GASP1) or GASP SEQ ID NO:6 (GASP2); and

(ii) a GASP polypeptide comprising SEQ ID NO:2 (GASP1) or SEQ ID NO:6 (GASP2) or an allelic or species variant thereof;

b) determining the level of:

(i) GASP polypeptide;

(ii) GASP RNA; or

(iii) agonist-induced down-regulation of the G protein-coupled receptor.

69. The screening method of claim 68, wherein said method additionally comprises recording any test agent that induces a difference in said level in a database of agents that inhibit or enhance agonist-induced down-regulation of the G protein-coupled receptor.

70. The screening method of claim 68, wherein the level of GASP polypeptide is determined.

71. The screening method of claim 68, wherein the level of GASP RNA is determined.

72. The screening method of claim 68, wherein the level of agonist-induced down-regulation of the G protein-coupled receptor is determined.

73. The screening method of claim 68, the cell is *in vitro*.

74. The screening method of claim 68, additionally comprising selecting a test agent that reduces the level of:

(i) GASP polypeptide;

(ii) GASP RNA; or

(iii) agonist-induced down-regulation of the G protein-coupled receptor.

as an inhibitor of agonist-induced down-regulation of the G protein-coupled receptor.

75. The screening method of claim 68, wherein said determining comprises determining the level of agonist-induced down-regulation of the G protein-coupled receptor by a radioligand binding assay.

76. The screening method of claim 68, additionally comprising selecting a test agent that increases the level of:

(i) GASP polypeptide;

(ii) GASP RNA; or

(iii) agonist-induced down-regulation of the G protein-coupled receptor

as an enhancer of agonist-induced down-regulation of the G protein-coupled receptor.

77. The screening method of claim 74 or 76, additionally comprising combining the inhibitor or enhancer, respectively, with a pharmaceutically acceptable carrier.

78. The screening method of claim77, additionally comprising combining the inhibitor or enhancer with an agonist of the G protein-coupled receptor.